UNITED STATES DEPARTMENT OF COMMERCE United States Patent and Trademark Office Address: COMMISSIONER FOR PATENTS P.O. Box 1450 Alexandria, Virginia 22313-1450 www.uspto.gov

| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|------------------------|---------------------------------|----------------------|----------------------|------------------|
| 10/581,975 | 05/23/2007 | Jack D. Newman | B04-020-2 (BERK-033) | 7227 |
| 84220 UC Berkeley - | 7590 08/06/200 OTL | EXAMINER | | |
| Bozicevic, Field | 1 & Francis LLP | GITOMER, RALPH J | | |
| East Palo Alto, | 7 Avenue, Suite 200 CA 94303 | | ART UNIT | PAPER NUMBER |
| , | | | 1657 | |
| | | | | |
| | | | MAIL DATE | DELIVERY MODE |
| | | | 08/06/2009 | PAPER |

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

| | | Applica | ition No. | Applicant(s) | Applicant(s) | | | | |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------|---------------------------|----------------|-------------------------------|---------------|--|--|--|--|
| | | 10/581 | ,975 | NEWMAN ET AL. | NEWMAN ET AL. | | | | |
| Office Action Summary | | | er | Art Unit | | | | | |
| | | Ralph G | Bitomer | 1657 | | | | | |
| | The MAILING DATE of this communication appears on the cover sheet with the correspondence address Period for Reply | | | | | | | | |
| A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION. - Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication. - If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication. - Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b). | | | | | | | | | |
| Status | | | | | | | | | |
| 1) 又 | Responsive to communication(s) file | ed on <i>28 June 2007</i> | | | | | | | |
| · · · · · · · · · · · · · · · · · · · | | 2b)⊠ This action is | | | | | | | |
| ′= | Since this application is in condition | / — | | atters, prosecution as to the | e merits is | | | | |
| ٠,ڪ | closed in accordance with the practice under <i>Ex parte Quayle</i> , 1935 C.D. 11, 453 O.G. 213. | | | | | | | | |
| Dispositi | on of Claims | | | | | | | | |
| 4)🖂 | Claim(s) <u>1-19</u> is/are pending in the | application. | | | | | | | |
| - | 4a) Of the above claim(s) is/are withdrawn from consideration. | | | | | | | | |
| | Claim(s) is/are allowed. | | | | | | | | |
| · | 6)⊠ Claim(s) <u>1-19</u> is/are rejected. | | | | | | | | |
| | Claim(s) is/are objected to. | | | | | | | | |
| - | Claim(s) are subject to restri | ction and/or electior | requirement. | | | | | | |
| Applicati | on Papers | | | | | | | | |
| 9)□ . | The specification is objected to by the | ne Examiner. | | | | | | | |
| ,— | The drawing(s) filed on is/are | | b)∏ objected t | o by the Examiner. | | | | | |
| / — | Applicant may not request that any obje | | | - | | | | | |
| | | | - | | FR 1.121(d). | | | | |
| Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d). 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152. | | | | | | | | | |
| Priority u | nder 35 U.S.C. § 119 | | | | | | | | |
| 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f). a) All b) Some * c) None of: 1. Certified copies of the priority documents have been received. | | | | | | | | | |
| 2. Certified copies of the priority documents have been received in Application No 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)). | | | | | | | | | |
| * See the attached detailed Office action for a list of the certified copies not received. | | | | | | | | | |
| Attachment | ` ' | | _ | | | | | | |
| 1) Notice of References Cited (PTO-892) 4) Interview Summary (PTO-413) Paper No(s) Mail Data | | | | | | | | | |
| 2) Notice of Draftsperson's Patent Drawing Review (PTO-948) 3) Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date 5) Notice of Informal Patent Application Other: | | | | | | | | | |

The IDS received 6/28/07 has been entered and claims 1-19 are currently pending in this application. Please inform the examiner of any related cases, abandoned, pending or allowed.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-19 are rejected under 35 U.S.C. 103(a) as being unpatentable over the combination of Garcia-Alles in view of Croteau.

Application/Control Number: 10/581,975

Page 3

Art Unit: 1657

Garcia-Alles (J of Biological Chemistry) entitled "Mechanism Based Inhibition of Enzyme I of the E. coli Phosphotransferase System" teaches in the abstract, a phosphotransferase is reacted with a suicide inhibitor and the result is identified by mass spec. On page 6935 column 2 last paragraph bridging to page 6936, the mass spec analysis is described.

The claims differ from Garcia-Alles in that they isolate the desired enzymes before reacting with the substrate.

Croteau (Archives of Biochemistry and Biophysics) entitled "Irreversible Inactivation of Monoterpene Cyclases by a Mechanism Based Inhibitor" teaches in the abstract enzymes are reacted with radiolabeled suicide substrates. On page 399 column 2 last full paragraph, the enzymes were purified by gradient elution from DEAE Sepharose Fast Flow from crude gland extracts.

It would have been obvious to one of ordinary skill in the art at the time of the invention to purify the enzymes of Garcia-Alles by any known method of enzyme purification such as those shown by Croteau because Garcia-Alles starts with already purified enzymes which would not require further isolation. Croteau performs much the same process as presently claimed from crude extracts which require purification prior to identification steps.

Regarding claims 5-8 directed to known methods of enzyme isolation, employing known methods of protein purification for their known function with the expected results would have been obvious. Regarding claims 17-19 once an enzyme has been identified, further useful processes such as nucleotide sequence determination, using hybridization probes and PCR are conventional in this art.

Claims 1-19 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for terpene synthase, does not reasonably provide enablement for "an enzyme". The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

In claim the terms "an enzyme" lack enablement as it would require one of ordinary skill in this art undue experimentation to determine which such enzyme would work in the instant invention.

The entire scope of the claims has not been enabled because:

- 1. Quantity of experimentation necessary would be undue because of the large proportion of inoperative enzymes claimed.
- 2. Amount of direction or guidance presented is insufficient to predict which enzymes encompassed by the claims would work.
- 3. Presence of working examples are only for a single specific type of enzyme and extension to other enzymes has not been specifically taught or suggested.
- 4. The nature of the invention is complex and unpredictable.

5. State of the prior art indicates that most related enzymes are not effective for the claimed functions.

- 6. Level of predictability of the art is very unpredictable.
- 7. Breadth of the claims encompasses an innumerable number of enzymes.
- 8. The level of one of ordinary skill in this art is variable.

In re Wands, 858 F.2d 731, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-19 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Each of the following applies in all occurrences.

In claim 1 line 2, "selected" is unclear as to how the substrate relates to the enzyme or how it was selected for what. In claim 1 line 3 "provides for" does not positively recite what occurs. In claim 3 "tandem mass spectrometry analysis" lacks antecedent basis. In claim 12 line 2, it is unclear if Markush terminology is intended.

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Janda (5,571,681) teaches suicide substrate conjugates.

Keasling (2003/0148479) teaches terpene syntheses.

Cane (Bioorganic & Medicinal Chemistry Letters) teaches synthase inhibition.

Application/Control Number: 10/581,975 Page 6

Art Unit: 1657

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ralph Gitomer whose telephone number is (571) 272-0916. The examiner can normally be reached on Monday - Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon Weber can be reached on (571) 272-0925. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Ralph Gitomer/ Primary Examiner, Art Unit 1657 Ralph Gitomer Primary Examiner Art Unit 1657